Article 13. – COMPOUNDING

68-13-1. (Authorized by K.S.A. 65-1630; implementing K.S.A. 2001 Supp. 65-1642; effective May 1, 1988; amended Feb. 7, 2003; revoked P-_____.)

68-13-2. Definitions. (a) "Beyond-use date" means a date placed on a prescription label at the time of dispensing, repackaging, or prepackaging that is intended to indicate to the patient or caregiver a time beyond which the contents of the prescription are not recommended to be used.

(b) "Biological safety cabinet" means a containment unit suitable for the preparation of low-risk to high-risk agents, when there is a need for protection of the product, personnel, and environment, that meets the requirements in national sanitation foundation standard 49, class II laminar flow biohazard cabinetry, as in effect on November 1, 2005, which standard is adopted by reference.

(c) "Component" means any ingredient intended for use in the compounding of a drug product, including any ingredient that does not necessarily appear in the list of ingredients for the drug product.

(d) "Compounding" means the combining of components into a compounded preparation under either of the following conditions:

(1) As the result of a practitioner's prescription drug order or initiative based on the practitioner-patient-pharmacist relationship in the course of professional practice; or

(2) for the purpose of, or incident to, research, teaching, or chemical analysis and not for sale or dispensing.

Compounding shall include the preparation of drugs or devices in anticipation of receiving prescription drug orders based on routine, regularly observed prescribing patterns. The reconstitution of oral or topical commercial products shall not be considered compounding for the purposes of this regulation.

(e) "Compounding area" means any area in a pharmacy where compounding is performed.

(f) "Cytotoxic," when used to describe a pharmaceutical, means that the pharmaceutical has the capability of killing living cells. This term shall also be used to describe components classified as cancer chemotherapeutic, carcinogenic, mutagenic, and antineoplastic.

(g) "Essentially a copy of a commercially available drug product" does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.

(h) "Inordinate amount" means in quantities that exceed 5 percent of the total prescription orders dispensed annually.

(i) "Order" means either a prescription order as defined in K.S.A. 65-1626(cc), and amendments thereto, or a medication order as defined in K.A.R. 68-5-1(c).

(j) "Practitioner-patient-pharmacist relationship" means a relationship that meets all of the following conditions:

(1) The practitioner has assumed the responsibility for making medical judgments regarding the health of the patient and the need for medical treatment.

(2) The practitioner has sufficient knowledge of the patient to initiate at least a general or preliminary diagnosis of the medical condition, and the practitioner has examined the patient and is available for follow-up.

(3) The practitioner has communicated the necessary prescriptions to the pharmacist, who is able to provide pharmaceutical care to the patient and communicate with the practitioner if needed.

(k) "Parenteral," when used to refer to a solution, means that the solution is administered by injection through one or more layers of skin.

(l) "Parenteral product" means a preparation administered by injection through one or more layers of skin. (Authorized by K.S.A. 65-1630; implementing K.S.A. 65-1634 and K.S.A. 2005 Supp. 65-1642; effective P-_____.)

68-13-3. Nonsterile compounded preparations. (a) This regulation shall apply to nonsterile compounded preparations compounded in Kansas and to nonsterile compounded preparations that are compounded outside Kansas and to be administered to any patient within Kansas.

(b) A pharmacist shall not prepare regularly or in inordinate amounts a nonsterile compounded preparation that is essentially a copy of a commercially available product.

(c) A pharmacist shall not prepare a nonsterile compounded preparation using any component that has been withdrawn from the market by the food and drug administration for safety reasons or is deemed unsafe by the food and drug administration and listed in the code of federal regulations.

(d) A pharmacist may prepare a nonsterile compounded preparation before receiving a valid order if the pharmacist has previously filled orders for the nonsterile preparation generated as part of an established practitioner-patient-pharmacist relationship, which demonstrates a need to prepare the nonsterile preparation before receiving an order, for the convenience of the patient.

(e) A pharmacist shall not offer any nonsterile compounded preparations to prescribing practitioners, pharmacists, or pharmacies for resale except in the course of professional practice for a prescribing practitioner to administer to an identifiable patient.

(f) Within each pharmacy in which compounding occurs, one area shall be designated as the principal compounding area, where all compounding shall take place. In addition to the principal compounding area, there may be one or more satellite compounding areas that are a

part of the same pharmacy. The principal compounding area and any satellites shall meet the following requirements:

(1) All compounding areas shall be well-lighted and well-ventilated with clean and sanitary surroundings, free of food and beverages that are devoted primarily to compounding. These areas shall provide the drugs, chemicals and devices with the necessary protection from deterioration due to light, heat, and evaporation and shall be arranged to protect all prescription drugs and devices from pilferage and ant other unauthorized removal.

(2) All components used in the compounding of drug products shall be stored in labeled containers in a clean, dry area or, if required, under proper refrigeration.

(3) A sink for hand and equipment washing shall be available and shall be equipped with hot and cold running water.

(4) Purified water shall be used for compounding nonsterile compounded preparations when formulations indicate the inclusion of water.

(g) For each nonsterile compounded preparation, a uniform, readily retrievable formulation record shall be maintained, documenting the following:

(1) The ingredients, quantities, strength, and dosage form of the preparation compounded;

(2) the equipment used to prepare the preparation and the mixing instructions;

(3) the container used in dispensing;

(4) the storage requirements;

(5) the beyond-use date to be assigned;

(6) quality control procedures, which may include monitoring the following:

(A) Capsule weight variation;

(B) adequacy of mixing to ensure uniformity and homogeneity; and

(C) clarity, completeness, or pH of solutions;

(7) the source of the formulation; and

(8) the name of the pharmacist who verified the accuracy of the formulation record and the date of verification.

(h) For each nonsterile compounded preparation, a compounding record shall be maintained on the original prescription or medication order or on a separate, uniform, readily retrievable record documenting the following:

(1) The name and strength of the preparation;

(2) the identifier used to distinguish the preparation's formulation record from other formulation records;

(3) the manufacturers, lot numbers, and expiration dates, if applicable, of each component;

(4) the total number of dosage units compounded;

(5) the name of the person, or persons, who prepared the preparation;

(6) the name of the pharmacist, pharmacy student, or intern working under the direct supervision and control of the pharmacist who verified the accuracy of the preparation;

(7) the date of compounding;

(8) the assigned internal identification number, if used;

(9) the assigned beyond-use date. In the absence of valid scientific stability information that is applicable for a component or the compounded preparation, the beyond-use date shall be established in accordance with the following criteria:

(A) For nonaqueous and solid formulation, either of the following:

(i) If a manufactured drug product is the source of the active ingredient, six months from the date of compounding or the time remaining until the manufactured drug product's expiration date, whichever is earlier; or

(ii) if a substance found in the United States Pharmacopeia –National Formulary is the source of an active ingredient, six months or the time remaining until the entity's expiration date, whichever is earlier;

(B) for water-containing formulations prepared from ingredients in solid form, not more than 14 days when stored under refrigeration; and

(C) for all other formulations, not greater than the intended duration of therapy or 30 days, whichever is earlier;

(10) the prescription number, if assigned; and

(11) the results of quality control procedures.

This compounding record and the corresponding formulation record specified in subsection (g) shall be retained and readily available for inspection by the board at the compounding pharmacy for at least five years.

(i) The pharmacist-in-charge shall be responsible for ensuring that, before performing delegated compounding, all supportive personnel are trained and can successfully demonstrate the following:

(1) Comprehensive knowledge of the pharmacy's standard operating procedures with regard to compounding as set forth in the policy and procedure manual;

(2) and familiarity with the compounding techniques used in the pharmacy. (Authorized by K.S.A. 65-1630; implementing K.S.A. 65-1634 and K.S.A. 2005 Supp. 65-1642; effective P- _____.)

68-13-4. Sterile compounded preparations. (a) This regulation shall apply to sterile compounded preparations that are compounded in Kansas and also to sterile compounded preparations that are compounded outside Kansas and to be administered to a patient within Kansas.

(b) Definitions. As used in this regulation, the following words shall have the meanings specified.

(1) "Barrier isolation chamber" means an apparatus that meets each of the following specifications:

(A) Is designed to provide an international standards organization class five environment for the preparation of sterile products;

(B) uses solid chamber walls rather than air movement to create a critical area for product handling;

(C) has a high efficiency particulate air (HEPA) filtration system that conditions the air flowing through the unit to remove initial airborne particles and airborne particles generated within the controlled environment; and

(D) has a means by which products are introduced into the critical area and people interact with the product being prepared within the apparatus without breaking the seals of the chamber walls.

(2) "Batch" means multiple sterile dosage units in a quantity greater than 24 that are compounded in a discrete process by the same individuals during one limited time period.

(3) "Class five environment" means an atmospheric environment that contains less than 3,520 particles of 0.5 microns in diameter per cubic meter of air.

(4) "Class seven environment" means an atmospheric environment that contains less than 352,000 particles of 0.5 microns in diameter per cubic meter of air.

(5) "Class eight environment" means an atmospheric environment that contains less than 3,520,000 particles of 0.5 microns in diameter per cubic meter of air.

(6) "Sterile Compounded preparation" means a drug dosage form that is free from living microorganism and the preparation has been compounded by a pharmacist, or a pharmacy technician, pharmacy student, or intern working under the direct supervision and control of the pharmacist. This term shall include a commercially prepared sterile drug dosage form that has been altered by a pharmacist.

(7) "Controlled area" means an area that is designated for preparing sterile compounded preparations and that provides a buffer between the surrounding environment and the critical area.

(8) "Critical area" means any area in the controlled area where components, compounded products, or containers are exposed to the environment.

(9) "Dosage unit" means the amount of a compounded sterile preparation that would be administered to or taken by one patient at one time.

(10) "Endotoxin" means a poisonous substance produced during the metabolism and growth of certain microorganisms that is confined inside the microorganisms and is released only when the microorganisms are broken down or die.

(11) "Immediate use" means a situation in which a preparation is compounded in a medical care facility pursuant to a medication order immediately before administration to the patient, is needed in an emergent situation, and is administered over a period that is less than 24 hours.

(12) "Laminar airflow hood" means an apparatus designed to provide a class five environment for the preparation of sterile products using air circulation in a defined direction that passes through a high-efficiency particulate air (HEPA) filter to remove the initial airborne particles and any airborne particles generated within the controlled environment.

(13) "Low risk," when used to describe compounded sterile preparations, means that the preparations meet the following conditions:

(A) In the absence of sterility testing,. is stored at room temperature and completely administered within 48 hours from preparation or stored under refrigeration for 14 days or less before complete administration to a patient over a period not to exceed 24 hours or is frozen for 45 days or less at -20° C or colder before complete administration to a patient over a period not to exceed 24 hours;

(B) is an unpreserved sterile preparation prepared for administration to one patient or a batch-prepared preparation containing suitable preservatives for administration to more than one patient; and

(C) is prepared by closed system aseptic transfer of sterile, nonpyrogenic, finished pharmaceuticals obtained from licensed manufacturers into sterile final containers obtained from licensed manufacturers.

This term shall apply to single-patient admixtures, single-patient ophthalmic preserved solutions, single-patient syringes without preservative used in 48 hours, and batch-filled syringes with preservatives.

(14)(A) "Medium-risk," when used to describe any compounded sterile preparations, means that the preparation meets one or more of the following conditions:

(i) In the absence of sterility testing, is stored at room temperature and administered beyond 30 hours after preparation, is stored under refrigeration for more than nine days, or is stored frozen at -20°C or colder for more than 45 days;

(ii) is batch-prepared without preservatives and is intended for use by more than one patient or for use by one patient on multiple occasions;

(iii) is created by a compounding process that includes complex aseptic manipulations other than the single-volume transfer;

(iv) does not contain broad-spectrum bacteriostatic substances and is administered over several days; or

(v) is compounded by complex or numerous manipulations of sterile ingredients obtained from licensed manufacturers in a sterile container obtained from a license manufacturer by using a closed-system aseptic transfer.

(B) This term shall apply to the following:

(i) preparations for use in a portable pump or reservoir over multiple days;

(ii) batch reconstituted antibiotics without preservatives;

(iii) batch prefilled syringes without preservatives; and

(iv) total parenteral nutrient solutions that are either made by gravity transfer of carbohydrates and amino acids into an empty container with the addition of sterile additives with a syringe and needle or that are mixed with an automatic compounding device.

(15)(A) "High risk," when used to describe a sterile compounded preparation, means that the preparation meets one or more of the following conditions:

(i) The preparation is compounded from nonsterile ingredients or with nonsterile containers or equipment before terminal sterilization.

(ii) The sterile ingredients or components of the preparation are exposed to air quality inferior to class five.

(iii) The nonsterile ingredients or components of the preparations are exposed to air quality inferior to class five for at least six hours before being sterilized.

(iv) The compounding pharmacist cannot verify from documentation received from the supplier or by direct examination that the chemical purity and content strength of the ingredients meet their original or compendial specifications.

(v) The compounded preparation has been either stored at room temperature and administered beyond 24 hours after preparation or stored under refrigeration greater than 3 days or stored frozen at -20°C or colder for more than 45 days, and sterility has not been confirmed by testing.

(B) This term shall apply to preparations including the following:

(i) Alum bladder irrigation solution;

(ii) any morphine preparation made from powder or tablets;

(iii) total parenteral nutrition solutions made from dried amino acids;

(iv) total parenteral nutrition solutions sterilized by final filtration; and

(v) autoclaved intravenous solutions.

(c) Any pharmacist may compound a sterile preparation before receiving a valid order if the pharmacist has previously filled orders for the sterile preparation generated as part of an established practitioner-patient-pharmacist relationship, demonstrating a need to prepare the sterile preparation before receiving an order for the convenience of the patient.

(d) A pharmacist shall not offer any compounded sterile preparations to prescribing practitioners, pharmacists, or pharmacies for resale except in the course of professional practice for a prescribing practitioner to administer to an individual patient. Each sterile compounded preparation provided to a prescribing practitioner shall be considered a high-risk product. The distribution of sterile compounded preparations without a practitioner-patient-pharmacist relationship shall be considered manufacturing.

(e) A pharmacist shall not prepare regularly or in inordinate amounts any sterile compounded preparation that is essentially a copy of a commercially available product.

(f) A pharmacist shall not prepare any sterile compounded preparation using components that have been withdrawn from the market by the food and drug administration for safety reasons or that are deemed unsafe by the food and drug administration as listed in the current code of federal regulations.

(g) Each pharmacist or pharmacy engaged in the preparation and compounding of sterile preparations shall have available the following resources:

(l) A laminar airflow hood, barrier isolation chamber, or other suitable class five environment that is currently certified by a licensed inspector to ensure aseptic conditions within the working area and which has the required documentation. The certification shall be current if it occurred within the previous six months, or on the date the devise was last moved to another location, which ever is less. The required documentation shall include:

(i) inspection certifications for the past five years, or since the date of installation, whichever is less;

(ii) a record of all prefilter maintenance;

(iii) a record of all high efficiency particulate air filter maintenance; and

(iv) a record of all disinfecting and cleaning;

(2) a sink;

(3) a refrigerator capable of maintaining a temperature of 2° to 8° C (36° to 46° F), and a freezer, if needed, capable of maintaining a temperature of -25° to -10° C (-13° F to 14° F). The temperature shall be monitored and recorded each business day. Each pharmacy with an electronic system that alerts the pharmacist to noncompliant temperatures shall be exempt from daily recording;

(4) the reference materials required by K.A.R. 68-2-12a and a current copy of a reference text on intravenous incompatibilities and stabilities. If an electronic library is provided, a workstation shall be readily available for use by pharmacy personnel, students, interns, and board personnel;

(5) a policy and procedure manual, with an annually documented review by the pharmacist-in-charge or designee, which shall include the following subjects:

(A) Sanitation;

(B) storage;

(C) dispensing;

(D) labeling;

(E) destruction and return of controlled substances;

(F) recordkeeping;

(G) recall procedures;

(H) responsibilities and duties of supportive personnel;

(I) aseptic compounding techniques; and

(J) ongoing evaluation procedures for all staff making the preparations; and

(6) supplies necessary for sterile product compounding.

(h) For each compounded sterile preparation, a uniform, readily retrievable formulation record shall be maintained, documenting the following:

(1) the quantities, strength, and dosage form of all components of the preparation compounded;

(2) the equipment used to prepare the preparation and the mixing instructions;

(3) the container used in dispensing;

(4) the storage requirements;

(5) the beyond-use date to be assigned;

(6) quality control procedures, which may include monitoring the following, if applicable:

(A) Adequacy of mixing to ensure uniformity and homogeneity;

(B) clarity, completeness, or pH of solutions;

(7) the sterilization methods;

(8) the source of the formulation; and

(9) the name of the pharmacist who verified the accuracy of the formulation record and date of verification.

(i) For each sterile compounded preparation, a compounding record shall be maintained on the original prescription or medication order, or on a separate, uniform, readily retrievable record documenting the following:

(1) The name and strength of the sterile compounded preparation;

(2) the formulation record reference for the compounded sterile preparation;

(3) the name of the manufacturer, lot numbers, and expiration dates, and if applicable, of each component;

(4) the total number of dosage units compounded;

(5) the name of the person or persons who compounded the sterile preparation;

(6) the name of the pharmacist, pharmacy student, or intern working under the direct supervision and control of the pharmacist who verified the accuracy of the preparation;

(7) the date of preparation;

(8) the assigned internal identification number, if applicable;

(9) the assigned beyond-use date. In the absence of valid scientific stability information that is applicable for a component or the sterile compounded preparation, the beyond-use date shall be established in accordance with the following criteria:

(A) For nonaqueous and solid formulations, one of the following:

(i) If the manufactured drug product is the source of the active ingredient, six months or the time remaining until the product's expiration date, whichever is earlier;

(ii) if a substance listed in the United States pharmacopeia - national formulary is the source of the active ingredient, six months or the time remaining until the entity's expiration date, whichever is earlier;

(B) for water-containing formulations prepared from ingredients in solid form, not more than 14 days when stored under refrigeration; or

(C) for all other formulations, not longer than the intended duration of therapy or 30 days, whichever is earlier;

(10) the prescription number, if applicable;

(11) the results of quality control procedures; and

(12) the results of the sterility testing and, if applicable, pyrogen testing for the batch, if applicable.

The compounding record and corresponding formulation record shall be retained for at least five years and readily available for inspection by the board in the pharmacy where prepared for at least five years.

Medical care facilities shall be required to generate a compounding record and a corresponding formulation record only when batch compounding.

(j) Each person involved in the preparation of any compounded sterile product shall wear garb in accordance with the gowning standards contained in the united states pharmacopeial convention, inc. united states pharmacopeial national formulary , chapter 797, in effect on November 1, 2005, which standards are incorporated by reference.

(k) All compounded sterile preparations shall be stored and delivered in a manner that is designed to maintain parenteral product stability.

(l) All compounded sterile preparations shall be prepared under aseptic conditions as follows.

(1) Each low-risk compounded sterile preparation shall be prepared in a class five critical area using technique to ensure sterility.

(2) Each medium-risk sterile compounded preparation shall be prepared in conformance with requirements for low-risk sterile compounded preparation and, if not using a barrier isolation chamber, shall have a class eight surrounding controlled area;

(3) Each high-risk sterile compounded preparation shall be prepared in conformance with the requirements for low-risk sterile compounded preparation, and, if not using a barrier isolation chamber, shall have a class seven surrounding controlled area. All nonsterile components shall meet USP and FDA standards for identity, purity, and endotoxin levels as verified by a pharmacist.

Requirements for the controlled area in subsection 1 of this regulation shall not take effect until January 1, 2007 or a new compounding area is constructed or the compounding area is remodeled, whichever occurs first.

(m) Each pharmacist engaged in the dispensing of compounded sterile preparations shall meet all labeling requirements under state and federal law. In addition, the label of each compounded sterile preparation shall contain the following information:

(1) The name and quantity of each component;

(2) a beyond-use date;

(3) a prescribed flow rate;

(4) the name or initials of the person who prepared the preparation; and

(5) any special storage instructions.

(n)(1) The pharmacist-in-charge and all personnel involved in compounding sterile preparations shall have practical or academic training in sterile product compounding, clean room technology, laminar flow technology, and quality assurance techniques. This training shall be documented for each person before that person begins to compound sterile products. That documentation shall be maintained by the pharmacy for five years and shall be made available to the board upon request.

(2) The pharmacist-in-charge shall be responsible for ensuring that all supportive personnel are trained and successfully demonstrate the following before performing any delegated sterile admixture services:

(A) Comprehensive knowledge of the pharmacy's standard operating procedures with regard to sterile admixture services, as set forth in the policy and procedure manual;

(B) familiarity with the compounding techniques; and

(C) aseptic technique, which shall be proven by means of a test batch.

This training shall be documented for each person before that person begins to compound sterile products. That documentation shall be maintained by the pharmacy for five years and shall be made available to the board upon request. Each individual who fails to demonstrate acceptable aseptic technique shall be prohibited from engaging in sterile product preparation until demonstrating acceptable technique by means of a test batch.

(3) The pharmacist-in-charge shall be responsible for testing the aseptic technique of all personnel involved in sterile product preparation annually by means of a test batch. All personnel involved in high-risk sterile product preparation shall undergo this testing biannually. The test results shall be maintained for five years and shall be made available for the board's inspection upon request. Each individual who fails to demonstrate acceptable aseptic technique shall be prohibited from engaging in sterile product preparation until demonstrating acceptable technique by means of a test batch. (Authorized by K.S.A. 65-1630; implementing K.S.A. 65-1634 and K.S.A. 2005 Supp. 65-1642; effective P-_____.)